Original article

Safety and efficacy in actual clinical practice of once-weekly subcutaneous teriparatide for osteoporosis patients with a high fracture risk

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ABSTRACT

Objectives: To reassess the safety and efficacy of once-weekly teriparatide 56.5 μg in osteoporosis patients with a high fracture risk.
Methods: This postmarketing observational study was conducted at 72 weeks according to the package insert. Of the 3573 Japanese osteoporosis patients in the safety analysis set, 91.80% were women, the mean age was 78.1 years, and 69.89% had a history of prevalent fragility fractures, indicating that a high proportion of patients at high risk of fracture were enrolled.
Results: Persistence with weekly teriparatide treatment was 59.36%, and 38.95% at 24 and 72 weeks, respectively. Adverse drug reactions (ADRs) were reported in 898 patients (25.13%), and serious ADRs were reported in 26 patients (0.73%). The most frequent ADRs were nausea, vomiting, and headache. The cumulative incidence of new vertebral fractures 72 weeks after the start of treatment was 3.31%. Increases in the bone mineral density were observed in the lumbar spine, femoral neck, and proximal femur. The serum levels of the bone formation markers, procollagen type I N-terminal propeptide and bone-type alkaline phosphatase, increased slightly at 24 weeks and then decreased to baseline levels. At 24 and 72 weeks, the bone resorption markers, serum cross-linked N-terminal telopeptide of type I collagen and urinary cross-linked N-terminal telopeptide of type I collagen, were the same as or slightly lower than at baseline. Visual analogue scale scores for low back pain also decreased.
Conclusions: The present results showed that once-weekly teriparatide may also be useful for osteoporosis patients with a high risk of fracture.

1. Introduction

Teriparatide, a daily self-injection formulation (Forteo, Eli Lilly and Co., Indianapolis, IN, USA), is widely used throughout the world as an osteoporosis medication that results in significant bone formation marker (procollagen type I N-terminal propeptide, P1NP) increases [1] and has a powerful effect in reducing vertebral fractures [2]. Meanwhile, in Japan, a once-weekly administered teriparatide formulation (Teribone, Asahi Kasei Pharma Corp., Tokyo, Japan) with a dosage and administration different from the above formulation is also already being used for the indication of osteoporosis in patients at high risk of fracture. In the Phase 3 Teriparatide Once-Weekly Efficacy Research (TOWER) trial, once-weekly administration of teriparatide 56.5 μg for 72 weeks resulted in an 80% reduction in the occurrence of new vertebral fractures compared with the placebo group, thus demonstrating the effect in reducing new vertebral fractures in osteoporosis patients at high risk of fracture [3]. The results of the TOWER trial also showed that the changes over time in bone turnover markers associated with once-weekly administration of teriparatide were clearly different from those associated with daily teriparatide administration. Specifically, daily teriparatide administration resulted in sustained and significant increases in the bone formation marker, serum P1NP, as well as somewhat slower sustained increases in the bone resorption marker, serum CTX (C-terminal telopeptides type I collagen) [4,5], whereas during once-weekly administration, it was reported

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that the serum P1NP increased 4 weeks after administration but then decreased, while there was more of a sustained trend toward a mild decrease in the bone resorption marker, urinary cross-linked N-terminal telopeptide of type I collagen (uNTX), compared with baseline [3,6]. The results thus show that once-weekly and daily administration of teriparatide are similarly highly effective in preventing osteoporotic vertebral fractures but may have different mechanisms of action and have different effects on bone turnover.

Because the TOWER trial was a phase 3 clinical study, patients diagnosed with secondary osteoporosis and patients who had received bisphosphonates in the past year were excluded based on the entry criteria because these conditions were highly likely to affect assessment of the incidence of fractures, so the patient characteristics in that study may differ somewhat from those of patients in actual clinical practice. Also, the number of patients was relatively small, resulting in very limited information on administration in male patients or patients with hepatic or renal disorders, and hardly any information on coadministration with other osteoporosis medications. As it was therefore considered important to demonstrate in a large-scale surveillance study the safety and efficacy of once-weekly administration of teriparatide in actual clinical practice after marketing, we conducted a postmarketing study, with a target sample size of 3000 patients, as a prospective observational study, the results of which are now being reported.

2. Methods

2.1. Study design

This surveillance was an observational study to confirm the efficacy and safety of once-weekly subcutaneous injections of 56.5-μg teriparatide in actual clinical practice after marketing. The surveillance was conducted as a prospective observational study using a system in which information on patients who started treatment with teriparatide 56.5 μg/wk was faxed by attending physicians to an enrollment center for enrollment within 7 days (including the administration start date), and treatment information was then reported in surveillance case report forms. The target sample size was 3000 patients, and the surveillance was conducted from December 2011 to November 2015. During the surveillance period, the enrollment period was from the beginning of the surveillance to November 2013.

The surveillance was conducted in accordance with the Good Postmarketing Study Practice Ordinance (Ministry of Health, Labour and Welfare Ordinance No. 171, December 20, 2004).

2.2. Subjects and treatment

The subjects of the surveillance were osteoporosis patients who, in the opinion of attending physicians, were at high risk of fractures based on risk for fractures such as low bone mineral density, history of fragility fractures, and age. Teriparatide 56.5 μg was subcutaneously injected once weekly, and the treatment period was up to 72 weeks, which was the administration limit at commercial launch.

2.3. Data collection

During the 72-week administration period, information from the start of administration until 24 weeks was collected in the first surveillance case report form, and information from 25 to 72 weeks was collected in the second surveillance case report form. The following were investigated as information on baseline characteristics: sex, age, height, weight, patient status (outpatient, inpatient, home visits/in-home care), osteoporosis classification (primary, secondary), history of fragility fractures etc., parental history of hip fracture, smoking history, alcohol intake, comorbidities and prior history, prior treatment medication, teriparatide treatment compliance as information on treatment compliance, and concomitant medication.

2.4. Safety

Among adverse events, including abnormal changes in laboratory values observed during the administration period, adverse events for which it was determined that a causal relationship to teriparatide could not be ruled out were assessed as adverse reactions. The preferred terms in MedDRA/J version 20.0 (MedDRA Japanese Maintenance Organization, Tokyo, Japan) were used to tabulate adverse reaction terms, and the type, incidence, and time of onset were checked.

2.5. Efficacy

When fragility fractures occurred during the administration period, the date of onset and location were tabulated. Information on the lumbar spine, femoral neck, and total hip (proximal femur) bone mineral density, as determined by dual-energy X-ray absorptiometry, was also collected every 24 weeks from the start of administration, and was tabulated as the percentage (%) relative to the Japanese young adult mean (YAM) [7]. Information on the following bone turnover markers was collected: serum undercarboxylated osteocalcin (ucOC), P1NP, BAP, NTX, and tartrate-resistant acid phosphate-5b (TRACP-5b), and uNTX. Information on the visual analogue scale (VAS) for low back pain was collected every 24 weeks from the start of administration in patients for whom such information was available. The precision of bone mineral density and bone turnover marker measurement was based on the control standards at each medical institution.

2.6. Statistical analysis

The mean and standard deviation were calculated for information on baseline characteristics such as age, height, and weight. The mean and 95% confidence interval are shown for the bone mineral density percentage relative to YAM at 24, 48, and 72 weeks after the start of administration, and the median, 1st quartile, and 3rd quartile are shown for bone turnover markers and the VAS. In this statistical analysis, the results at 24, 48, and 72 weeks were compared with baseline using the Wilcoxon signed-rank test. The number and percentage of patients were calculated for categorical data. Treatment continuation and the incidence of new fractures were calculated using the Kaplan-Meier estimation method. All statistical analysis was performed using SAS ver. 9.1.3 (SAS Institute, Cary, NC, USA).

3. Results

3.1. Number of patients

During the surveillance period, 3754 subjects were enrolled, and 104 subjects were excluded from enrollment because of, for example, violations in contract period or number of contracted subjects, resulting in 3650 effectively enrolled subjects, from whom 3626 surveillance case report forms were collected. Thirty-three subjects who violated the patient enrollment criteria for reasons such as conduct of the surveillance at a noncontracted medical institution or failure to enroll within 7 days of the start of teriparatide administration were excluded, and the results are shown for the 3573 patients who received teriparatide administration for the first time in this surveillance among the 3593 subjects of the

resulting safety analysis set. Of these 3593 subjects, 209 subjects were excluded because no efficacy information was obtained after administration, and 2 subjects were excluded due to suspicion of a disease other than osteoporosis (off-label use); the remaining 3362 subjects were used as the efficacy analysis set.

3.2. Baseline patient characteristics

Table 1 shows the patient characteristics. Most patients were women (91.80%), the mean (±standard deviation [SD]) age was 78.1 ± 7.8 years, 95.47% of patients were 65 years of age or older, 70.67% were 75 years of age or older, and the mean (±SD) body weight was 47.6 ± 8.8 kg. Osteoporosis was classified as primary osteoporosis in 92.89% of patients and as secondary osteoporosis in 6.86% of patients. There was a past history of fragility fractures in 69.89% of patients, a past history of vertebral fractures in 61.10% of patients, and a past history of femur fractures in 7.00% of patients. Bone mineral density was measured at baseline in the lumbar spine in 1524 patients, femoral neck in 1096 patients, and total hip (proximal femur) in 372 patients. In these patients, the bone mineral density was <70% of YAM in 63.98% of patients (lumbar spine), 75.91% of patients (femoral neck), and 71.77% of patients (total hip [proximal femur]), respectively. Renal disorders were reported in 2.52% of patients (90 patients), and hepatic disorders were reported in 2.57% of patients (92 patients).

3.3. Teriparatide treatment compliance

The percentage of subjects who continued teriparatide treatment, based on the Kaplan-Meier estimation method, was 59.36% at 24 weeks and 38.95% at 72 weeks (Fig. 1A). Of the 2260 patients who discontinued teriparatide administration, treatment was discontinued within 24 weeks in 1596 patients, and the most common reasons for discontinuation were adverse events in 36.34% of patients, patient failure to visit in 33.40% of patients, and transfer to other hospital or change in residence in 19.24% of patients. Treatment was discontinued after 24 weeks but before 72 weeks in 664 patients, and the most common reasons were patient failure to visit in 34.79% of patients, adverse events in 23.80% of patients, and transfer to other hospital or change in residence in 17.62% of patients.

Concomitant osteoporosis medication was used in 930 patients (26.03%); the most common medications were active vitamin D preparations in 586 patients (63.01%), bisphosphonates in 183 patients (19.68%), calcium preparations in 180 patients (19.35%), SERMs in 116 patients (12.47%), vitamin K preparations in 92 patients (9.89%), and anti-receptor activator of nuclear factor κB ligand (RANKL) antibody in 7 patients (0.75%).

3.4. Safety

Adverse reactions occurred in 898 of the 3573 patients (25.13%) in the safety analysis set. The most common adverse reactions were nausea (12.31%), vomiting (2.77%), headache (2.74%), dizziness (2.16%), malaise (1.85%), feeling abnormal (1.82%), and pyrexia (1.46%) (Table 2). Serious adverse reactions were reported in 26 of the 3573 patients (0.73%); the most common serious adverse reactions were cerebral infarction, depressed level of consciousness, dizziness, cardiac failure, and vomiting. The time of the initial onset of adverse reactions was within 24 weeks in 777 of the 898 patients with adverse reactions (86.53%), indicating that most occurred within 24 weeks.

Table 1
Characteristics of patients in the safety analysis set (n = 3573).

Characteristic	Value
Sex	
Male	293 (8.20)
Female	3280 (91.80)
Age, yr	
Mean ± SD, %	78.1 ± 7.8
Median (range)	79.0 (27.0−104.0)
<65	162 (4.53)
≥65, <75	886 (24.80)
≥75, <85	1813 (50.74)
≥85	712 (19.93)
BMI, kg/m^2	
BMI measurements, n	2934
<17	227 (7.74)
≥17, <18.5	294 (10.02)
≥18.5, <25	1955 (66.63)
≥25, <30	413 (14.08)
≥30	45 (1.53)
Patient category	
Outpatient	3170 (88.72)
Inpatient	381 (10.66)
House call/visiting care (home care, etc.)	22 (0.62)
Osteoporosis classification	
Primary	3319 (92.89)
Secondary	245 (6.86)
Unknown	9 (0.25)
BMD (percentage of YAM) lumbar spine	
BMD measurements, n	1524
Mean ± SD, %	66.5 ± 15.5
<70	975 (63.98)[a]
≥70	549 (36.02)[a]
BMD (percentage of YAM) in the femur (neck)	
BMD measurements, n	1096
Mean ± SD	62.7 ± 13.3
<70	832 (75.91)[a]
≥70	264 (24.09)[a]
BMD (percentage of YAM) in the femur (proximal total)	
BMD measurements, n	372
Mean ± SD	63.1 ± 12.3
<70	267 (71.77)[a]
≥70	105 (28.23)[a]
History of fragility fracture (with overlap)	
History of fragility fracture	2497 (69.89)
History of vertebral fracture	2183 (61.10)
History of nonvertebral fracture	644 (18.02)
History of proximal femoral fracture	250 (7.00)
Parent's history of fragility fracture of the proximal femur	105 (2.94)
History of current smoking: yes	134 (3.75)
Alcohol intake history (≥3 units/day): yes, 1 unit: ethanol 8−10 g	108 (3.02)
Complications (with overlap)	
Patients with disease at the start of treatment	2364 (66.16)
Renal impairment	90 (2.52)
Hepatic impairment	92 (2.57)
Severity of chronic kidney disease in patients with renal dysfunction eGFR, mL/min/1.73 m^2[b]	
≥90	17 (0.78)[c]
≥60, <90	415 (19.01)[c]
≥45, <60	1045 (47.87)[c]
≥30, <45	600 (27.49)[c]
≥15, <30	93 (4.26)[c]
<15	13 (0.60)[c]
Patients with a history of previous use of therapeutic agents for osteoporosis	1135 (31.77)
Breakdown (with some overlap)	
Bisphosphonates	772 (68.02)[d]
Active vitamin D preparations	417 (36.74)[d]
SERM	140 (12.33)[d]
Calcium preparations	46 (4.05)[d]
Teriparatide formulation other than Teribone	24 (2.11)[d]
Vitamin K preparations	18 (1.59)[d]

Table 1 (continued)

Characteristic	Value
Anti-RANKL antibody	1 (0.09)[d]

Values are presented as number (%) unless otherwise indicated.
SD, standard deviation; BMI, body mass index; BMD, bone mineral density; YAM, young adult mean; SERM, selective estrogen receptor modulator.

[a] Percentage based on BMD tests of lumbar spine in 1524 patients, femoral neck in 1096 patients, and total hip (proximal femur) in 372 patients.

[b] Glomerular filtration rate as a percentage of that of a healthy young adult (Clinical Practice Guidebook for Diagnosis and Treatment of Chronic Kidney Disease 2012, edited by the Japanese Society of Nephrology [Chronic Kidney Disease Guidelines 2012 −Kidney Disease: Improving Global Outcomes−] modified for Japanese patients).

[c] Percentage based on the 2183 patients whose renal function was tested.

[d] Percentage based on the 1135 patients with a history of previous use of therapeutic agents for osteoporosis. Anti-RANKL, anti-receptor activator of nuclear factor κB ligand.

The incidence of adverse reactions was 16.38% in men (48 of 293 patients), which was lower than the incidence of 25.91% in women (850 of 3280 patients). There were no adverse reactions characteristic of men; frequently occurring adverse reactions included nausea, feeling abnormal, and pyrexia, which were also frequently occurring adverse reactions in women. Ninety patients had renal impairment, and the incidence of adverse reactions in these patients was 16.67% (15 of 90 patients), which was not higher than the overall adverse reaction incidence of 25.13% (898 of 3573 patients). Analysis of the incidence of adverse reactions by renal impairment severity revealed no categories with a particularly high incidence of adverse reactions (data not shown).

The most common adverse reactions occurring in patients with renal impairment were nausea, vomiting, and pyrexia, the same as in the overall adverse reaction profile. No renal impairment-related adverse reactions occurred.

Ninety-two patients had hepatic impairment, and the incidence of adverse reactions in these patients was 26.09% (24 of 92 patients), which was not significantly different compared with the overall adverse reaction incidence. The most common adverse reactions occurring in patients with hepatic impairment were nausea and pyrexia, which were frequently occurring adverse reactions overall, revealing no adverse reactions characteristic of patients with hepatic impairment. Two events of hepatic function abnormal were reported as hepatobiliary disorder-related adverse reactions.

The incidence of adverse reactions in patients using concomitant osteoporosis medication was 27.20% (253 of 930 patients), which was about the same as the adverse reaction incidence of 24.40% (645 of 2643 patients) in patients who used no concomitant osteoporosis medication and the adverse reaction incidence of 23.82% (277 of 1163 patients) in patients who used no concomitant medication. The incidence of adverse reactions was 26.79% (157 of
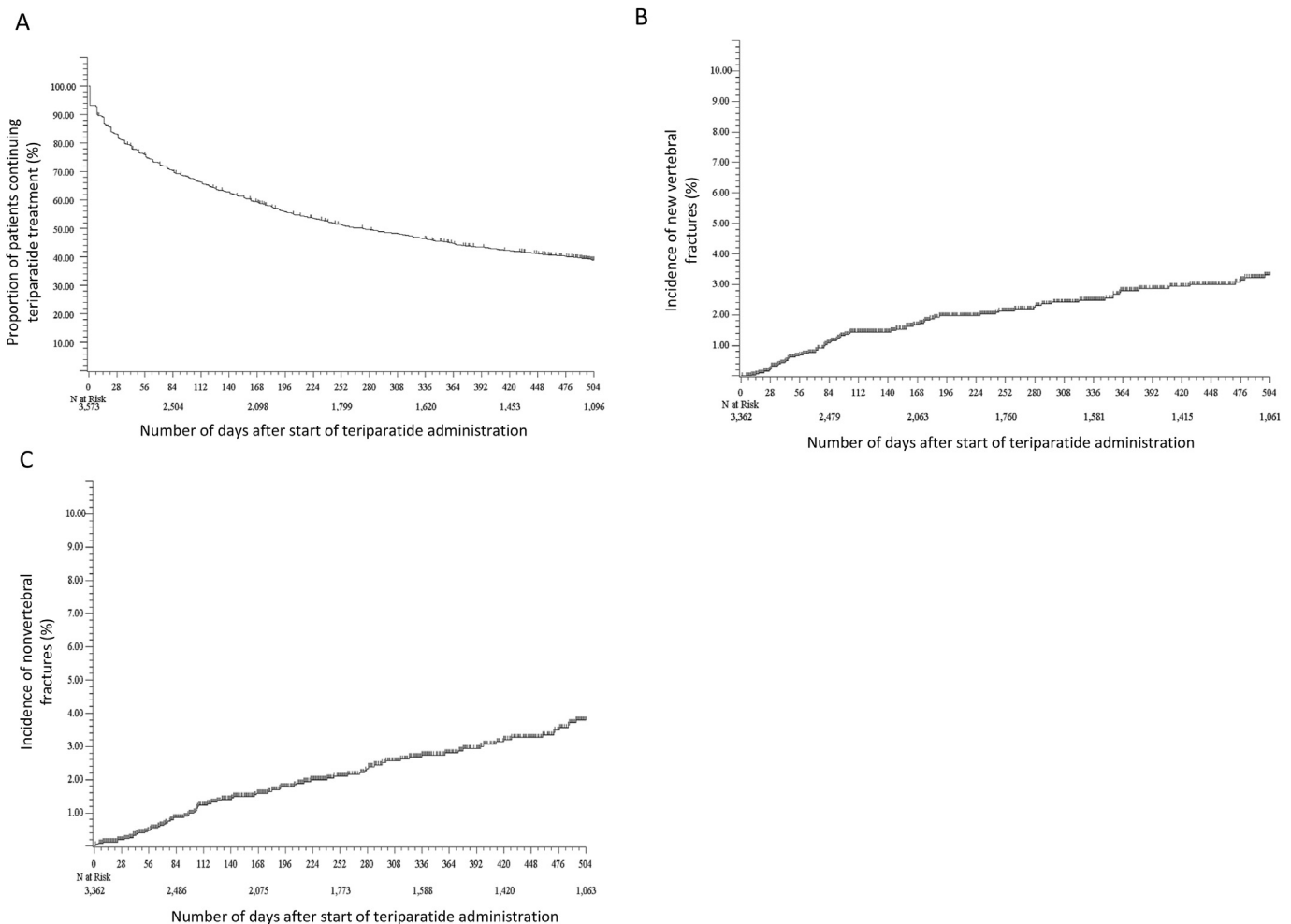
Fig. 1. Teriparatide treatment continuation and fracture incidence. (A) Teriparatide treatment continuation: Kaplan-Meier estimation method. (B) Incidence of new vertebral fractures: Kaplan-Meier estimation method. (C) Incidence of nonvertebral fractures: Kaplan-Meier estimation method.

Table 2
Adverse drug reactions observed in at least 10 patients (3573 patients in total).

Adverse drug reaction	No. of patients (%)
No. of patients with adverse reactions	898 (25.13)
Adverse drug reaction	
Nausea	440 (12.31)
Vomiting	99 (2.77)
Headache	98 (2.74)
Dizziness	77 (2.16)
Malaise	66 (1.85)
Feeling abnormal	65 (1.82)
Pyrexia	52 (1.46)
Decreased appetite	35 (0.98)
Palpitations	32 (0.90)
Chills	20 (0.56)
Blood pressure decreased	16 (0.45)
Abdominal discomfort	14 (0.39)
Diarrhea	11 (0.31)
Tremor	11 (0.31)
Flushing	11 (0.31)
Hotflush	11 (0.31)
Back pain	11 (0.31)
Somnolence	10 (0.28)

586 patients) in patients who used concomitant active vitamin D preparations and was 27.87% (51 of 183 patients) in patients who used concomitant bisphosphonates; analysis by type of osteoporosis medication revealed no medications with a particularly high incidence.

3.5. Efficacy

The incidence of new vertebral fractures at 24, 48, and 72 weeks, based on the Kaplan-Meier estimation method, in the 3362 patients of the efficacy analysis set was 1.68%, 2.48%, and 3.31%, respectively (Fig. 1B), and the incidence of nonvertebral fractures at those time points was 1.59%, 2.74%, and 3.79%, respectively (Fig. 1C). The percent change in bone mineral density, the change over time in bone turnover markers, and the change in VAS were analyzed in patients with measurements before and after (at any of the 24-, 48-, and 72-week time points) administration. Analysis of the percent change in bone mineral density relative to YAM at 24, 48, and 72 weeks showed a 2.8%, 4.9%, and 6.1% increase, respectively, in lumbar spine bone mineral density, a 1.6%, 1.4%, and 2.5% increase, respectively, in femoral neck bone mineral density, and a 1.0%, 1.6%, and 2.5% increase, respectively, in total hip (proximal femur) bone mineral density (Fig. 2).

The median percent change in serum P1NP increased 23.0% at 24 weeks compared with baseline and then decreased, showing minor increases of 4.3% at 48 weeks and 8.7% at 72 weeks (Fig. 3). The median percent change in serum BAP after 24 weeks was higher than at baseline but was about the same as at baseline after 48 weeks and 72 weeks. The median percent change in serum TRACP-5b and serum NTX was either no different from or lower than baseline at all time points. There were no obvious changes in uNTX throughout the administration period. The serum ucOC showed an approximately 50% increase compared with baseline at 24 and 48 weeks but only a 16.5% increase compared with baseline at 72 weeks.

The median change in VAS was −20, −25, and −28 compared with baseline at 24, 48, and 72 weeks, respectively, revealing improvement throughout the administration period (Fig. 4).

New vertebral fractures occurred in 2 of the 88 patients with hepatic impairment but there were no nonvertebral fractures; new vertebral fractures occurred in 4 of the 84 patients with renal impairment, and nonvertebral fractures occurred in 2 patients. New vertebral fractures occurred in 9 of the 278 male patients, and nonvertebral fractures occurred in 3 patients. Although all of these characteristics were analyzed in only a small number of patients, within the extent to which data were collected in this surveillance, efficacy did not appear to be affected by the presence or absence of hepatic impairment, the presence or absence of renal impairment, or sex.
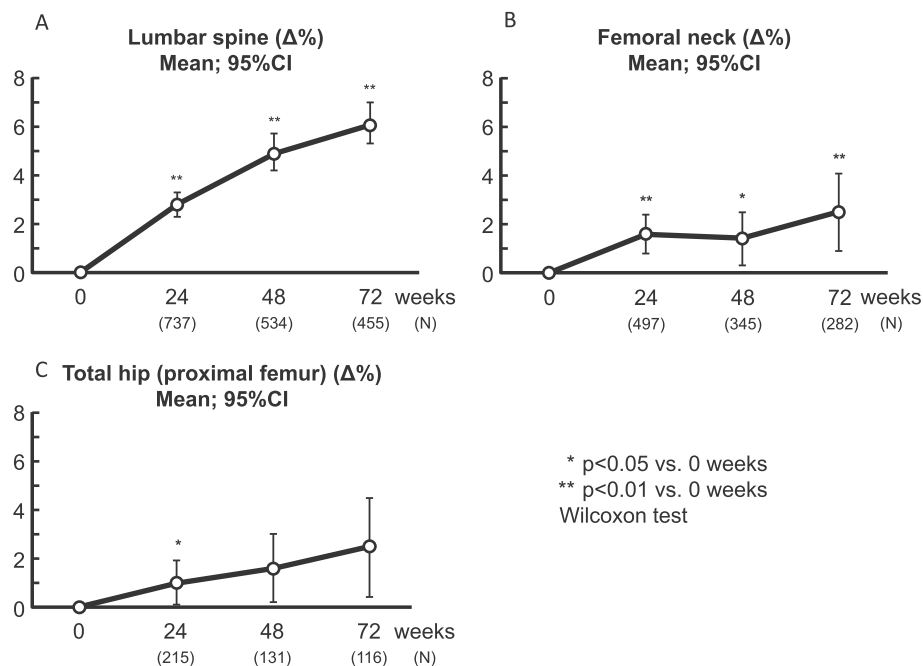

Fig. 2. Percent change from baseline in bone mineral density (BMD) (mean, 95% CI) after up to 72 weeks of teriparatide treatment in patients with osteoporosis at high risk of fracture in Japan. BMD was measured at the lumbar spine (A), femoral neck (B), and total hip (C). CI, confidence interval. *P < 0.05, **P < 0.01 for the increase from baseline at each time point.
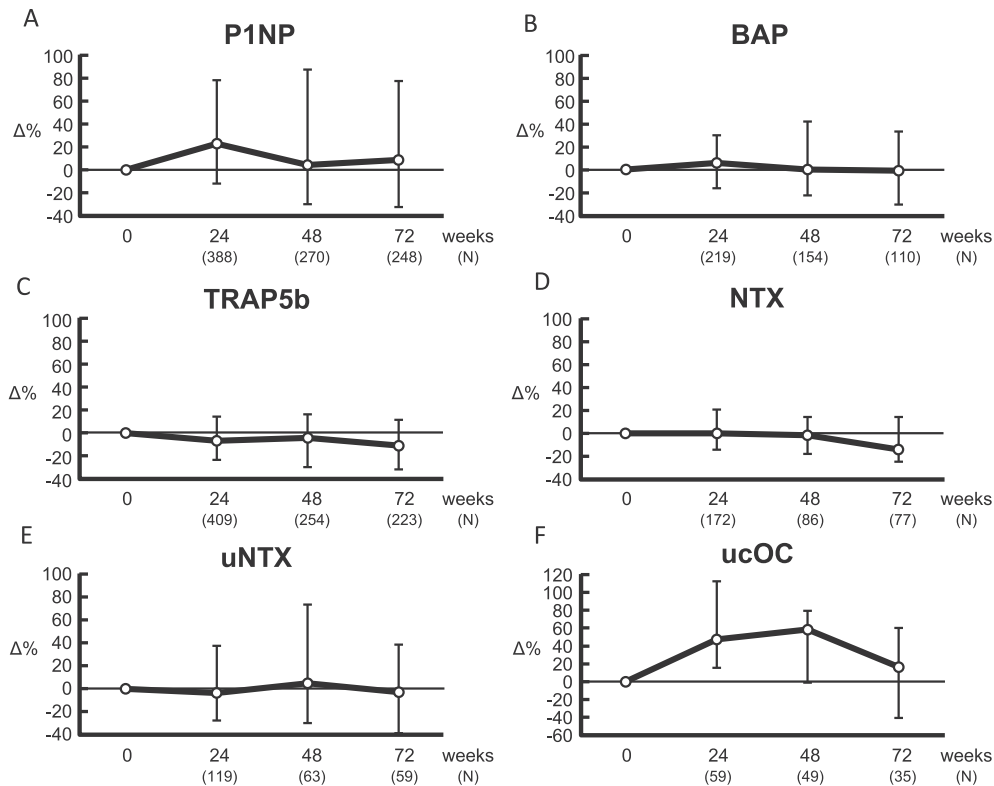
Fig. 3. Percent change from baseline in the P1NP (A) and BAP (B) biomarkers of bone turnover, TRACP-5b (C), NTX (D), uNTX (E) as biomarkers of bone resorption, and ucOC (F) as a biomarker of bone quality (median, Q1, Q3) after up to 72 weeks of teriparatide treatment in patients with osteoporosis at high risk of fracture in Japan. The mean (standard deviation) baseline values were: P1NP 47.9 (37.2) ng/L; BAP 16.5 (8.8) U/L; TRACP-5b 4.5 (2.2) U/L; NTX 20.2 (9.2) nmolBCE/L; uNTX 93.8 (171.4) nmolBCE/mmol·Cr; and ucOC 5.2 (7.1) ng/mL. P1NP, procollagen type I N-terminal propeptide; BAP, bone-type alkaline phosphatase; TRACP-5b, tartrate-resistant acid phosphatase 5b; NTX, cross-linked N-terminal telopeptide of type I collagen; uNTX, urinary NTX; ucOC, undercarboxylated osteocalcin
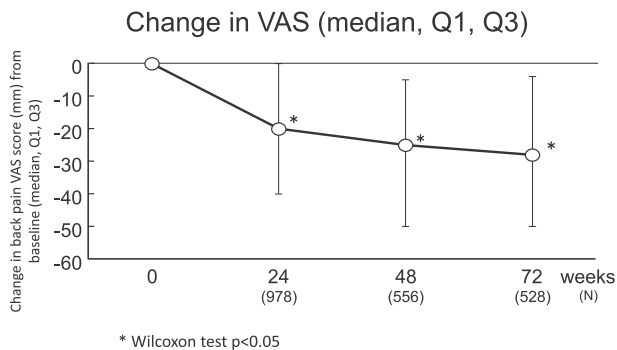
Fig. 4. Changes over time in change in visual analogue scale (VAS, mm) for low back pain (median, Q1, Q3). Q1, first quartile; Q3, third quartile.

4. Discussion

We analyzed the results of this postmarketing prospective observational study on the safety and efficacy of once-weekly subcutaneous injections of teriparatide 56.5 μg for the treatment of patients with osteoporosis at high risk of fracture in actual clinical practice.

In this surveillance, information on the risk of fracture collected by physicians during observation was collected in order to check whether teriparatide was used properly in patients at high risk of fracture. In this information on risks for facture, factors such as advanced age, prior history of fragility fractures, and low bone mineral density were reported as important risks for fracture [8,9].

In the patients for whom information was collected, 95.47% were 65 years of age or older, 70.67% were 75 years of age or older, and 69.89% had a prior history of fragility fractures. Furthermore, lumbar spine bone mineral density was measured in 42.65% of patients (1524 of 3573 patients), the mean percentage of which relative to YAM was 66.5%. These results show that most patients in this surveillance were at high risk of fracture.

The incidence of adverse reactions in this surveillance was 25.13% (898 of 3573 patients), which was not higher than the adverse reaction incidence of 43.8% (127 of 290 patients) in the TOWER trial.

The most common adverse reactions in this surveillance were nausea, vomiting, headache, and dizziness, indicating the same trend as frequently occurring adverse reactions in the TOWER trial.

The incidence of serious adverse reactions in this surveillance was 0.73% (26 of 3573 patients), and the time of onset was soon after the start of administration. Based on these results, the analysis of safety in actual clinical practice in the present surveillance revealed no significant differences from that in the clinical trial. Teriparatide was also administered to patients with hepatic impairment, patients with renal impairment, and men, which are populations for which information was limited in past analysis, but it was reported that no new efficacy or noteworthy safety findings on bone mineral density or bone turnover markers were observed in post hoc analysis of patients with stage 4 or 5 chronic kidney disease in a Japanese postmarketing study of the daily teriparatide formulation in patients with renal impairment [10]. There were no differences in the overall adverse reaction profile in patients with renal impairment in this surveillance. Within the extent to which data were collected in this surveillance, the incidence of adverse

reactions also was not significantly affected by the presence or absence of hepatic impairment or by sex. The above results revealed no particular safety concerns associated with the administration of teriparatide in patients with these special characteristics.

Although differences in the methods of assessment do not permit simple comparison of new vertebral fractures in the results for efficacy in this surveillance, the fracture incidences of 1.68%, 2.48%, and 3.31% at the 24-, 48-, and 72-week time points, respectively, were not significantly higher than the incidences of 2.6%, 3.1%, and 3.1% [3] in the TOWER trial. There were significant increases in lumbar spine and femoral neck bone mineral density compared with baseline from 24 weeks onward. The trend toward greater increases in lumbar spine bone mineral density than in femoral bone mineral density was similar to that reported during past once-weekly teriparatide administration. Characteristics of bone formation marker activity were observed in the TOWER trial [3] and in a 24-week trial that focused on the changes in bone turnover markers [6]. Specifically, there were increases up to 4 weeks after the start of administration and then gradual decreases. In the present surveillance, data were collected at 4 time points (baseline and 24, 48, and 72 weeks), making it impossible to confirm detailed changes in markers at time points up to 24 weeks. However, the changes in bone turnover markers from 24 weeks onward were generally the same as reported in the TOWER trial, etc.

With regard to the analgesic effect of teriparatide, it has been reported that the VAS of low back pain in patients with fresh osteoporotic vertebral fractures was significantly lower in daily and once-weekly teriparatide administration compared with risedronate [11]. Improvement in pain by teriparatide has furthermore been reported, for example, in a meta-analysis [12] and in osteoporosis animal models [13].

The results of the present surveillance also showed that the median change in VAS for low back pain at all time points was improved compared with baseline, suggesting that teriparatide may alleviate low back pain associated with osteoporosis. However, the mechanism of action is not fully understood, and may be a topic for future inquiry.

5. Conclusions

The above results indicate that once-weekly subcutaneous injections of teriparatide 56.5 μg were administered to appropriate patients in actual clinical practice. It was also confirmed that the results for safety were the same as in the clinical studies prior to approval. In addition, the results for efficacy parameters, including fracture incidences, in this surveillance were as expected based on the clinical studies prior to approval, indicating that the medical benefits of teriparatide were demonstrated in actual clinical practice after marketing.

Conflicts of interest

The authors are all employees of Asahi Kasei Pharma Corporation. Except for that, no potential conflict of interest relevant to this article was reported.

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